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Applicants' are *prima facie* entitled to a judgment relative to the patentee of the '497 and '007 patents.

II. Status Of The Claims And Support For The Amendment

Although the Office Action is final, a Request for Continued Examination is filed herewith. Accordingly, Applicants request that the finality of the Office Action be withdrawn, and that this amendment be entered.

Claims 27-29, 32, 58, 60, 61 and 64 have been amended, and new claims 65-67 have been added. Claims 27-32, 57, 58 and 60-67 are active in this application.

Support for the amendment of claims 27, 28, 32 and 60 is found in the specification at page 4, line 7.

Support for the amendment of claim 61 is found in the specification at page 4, line 21.

Support for the amendment of claim 64 is found in the specification at page 8, line 19.

Support for new claims 65 and 66 is found in the specification at page 4, line 21.

Support for new claim 67 is found in the specification at page 9, lines 19-20.

No new matter has been added by this amendment.

III. The Rejection Under 35 U.S.C. § 112 Must Be Withdrawn

At page 2 of the Office Action, the Examiner rejected claim 64 as indefinite, because claim 64 lacks antecedent basis in claim 63 for the term "preservative" [claim 63 uses the term "compound"]. Applicants respectfully traverse this rejection.

Claim 64 has been amended to replace the word "preservative" with "compound." Accordingly, it is believed that the ground for this rejection has been resolved by amendment, and Applicants respectfully request that this rejection be withdrawn.

IV. The Rejections Under 35 U.S.C. § 102(e) Must Be Reconsidered

At page 3 of the Office Action, the Examiner rejected claims 27-32, 57, 58 and 60-64 as allegedly anticipated by either the '497 patent or the '007 patent. Applicants respectfully traverse these rejections.

Filed herewith are a (1) Request For Interference under rule 607(a), (2) evidence in the form of 5 declarations and 16 documentary exhibits which constitute evidence demonstrating that Applicants are *prima facie* entitled to a judgment relative to effective filing date of the '497 and '007 patents, and (3) an explanation stating with particularity the basis upon which Applicants are entitled to a judgment relative to the effective filing date of the Patentee.

The evidence filed herewith establishes that Applicants (a) reduced to practice before the Patentee of the '497 and '007 patents, and/or (b) conceived prior to the Patentee of the '497 and '007 patents, and were diligent in reducing to practice from September 16, 1993 until October 13, 1993.

V. European And Australian Patent Opposition Proceedings

The '497 and '007 patents are assigned to Novo Nordisk A/S ("the Patentee"). Eli Lilly and Company ("Lilly") is the assignee of the present patent application. In 1997, Lilly filed a notice of opposition against the Patentee's Australian patent application no. 682061, from which Australian patent no. 682061 B2 issued. The grounds for opposition cited by Lilly included lack of novelty and lack of inventive step. The Australian opposition proceeding was resolved in 2000 in favor of the Patentee. Lilly's notice of opposition and the Australian Patent Office's opinion are listed in the PTO Form 1449 filed herewith, and a copy of each document is filed herewith.

In May, 2001, Lilly filed a notice of opposition against the Patentee's European patent no. 792 290 B1. The grounds for opposition cited by Lilly included lack of novelty, lack

of inventive step, and insufficiency of disclosure. The Patentee filed its response to the notice of opposition on March 24, 2003, and the European opposition proceeding is pending. Lilly's notice of opposition and the Patentee's reply are listed in the PTO Form 1449 filed herewith, and a copy of each document is filed herewith.

VI. Claims Herein Encompass A Composition Comprising A Fatty Acid-Acylated des(B30) Insulin Analog And Zinc

Claims 27 and 28 have been amended to cover des(B30) insulin analogs. A "des(B30)" insulin analog is an analog in which the amino acid residue at position 30 of the insulin B-chain is absent.[1] Specifically, claims 27 and 28 have been amended to recite "or a fatty acid-acylated insulin analog in which the amino acid residue at position B30 is Thr, Ala or deleted."

At page 2 of the Office Action, the Examiner confirmed that the rule 131 declaration filed on August 21, 1998 was sufficient to overcome Baker *et al.*, U.S. patent no. 5,693,609 ("the '609 patent"), and that the '609 patent would not be applied against claims 61-64 of the present application. The Examiner also noted "applicant's prior argument that the instant specification narrowly defines 'insulin' to be directed to normal or naturally occurring insulin from beef, pork and human and does not encompass acylated analogs and that the teachings of the '609 patent are directed to acylated analogs and not acylated normal or naturally occurring insulin from beef, pork, and human."

To the extent that the '609 patent discusses insulin analogs, an insulin analog is defined to be "a fast-acting insulin analog that is less prone to dimerization of self-association." *See* the '609 patent at column 4, lines 44-46.

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[1] The '497 and '007 patents disclose des(b30) analogs. *See* the '497 patent at column 3, line 25; the des(b30) analogs listed in columns 6-10; and example 11. *See* the '007 patent at

However, the '609 patent fails to disclose an acylated des(B30) insulin analog. Thus, the '609 patent by Baker *et al.* is not applicable to the claims in the present application.

VII. Complete Reply To Office Action

It is believed that this reply, and the evidence and the explanation under 37 C.F.R. § 608(b) filed herewith, are fully responsive to the Office Action.

Claim 64 has been amended to obviate the outstanding rejection for indefiniteness. Accordingly, Applicants respectfully request that this rejection be withdrawn.

With respect to the outstanding rejections under 35 U.S.C. § 102(e), the evidence and the explanation under 37 C.F.R. § 608(b) filed herewith establish that Applicants (a) reduced to practice prior to the Patentee of the '497 and '007 patents, and/or (b) conceived prior to the Patentee of the '497 and '007 patents, and were diligent in reducing to practice from September 16, 1993 until October 13, 1993.

Accordingly, Applicants respectfully request that the Examiner acknowledge that Applicants are entitled to a *prima facie* judgment of priority of invention relative to the Patentee, and pass this application to the Board of Patent Appeals and Interferences for declaration of an interference.

Respectfully submitted,

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April 24, 2003

column 3, line 38; and the des(B30) analogs listed in columns 6-10; and example 11.

VERSION OF CLAIMS WITH CHANGES SHOWN

27. (Once Amended) A composition comprising

(a) a fatty acid-acylated insulin or a fatty acid-acylated insulin analog in which the amino acid residue at position B30 is Thr, Ala or deleted, and

(b) zinc.

28. (Once Amended) A composition comprising an aqueous solution of

(a) a fatty acid-acylated insulin or a fatty acid-acylated insulin analog in which the amino acid residue at position B30 is Thr, Ala or deleted, and

(b) zinc.

29. (Once Amended) The composition of Claim 28, wherein the solution comprises about 0.2 mole to about 0.7 mole of zinc per mole of fatty acid-acylated insulin or fatty acid-acylated insulin analog.

32. (Once Amended) The composition of Claim 31, wherein the fatty acid-acylated insulin is N-acylated Lys^{B29} human insulin, and wherein the fatty acid-acylated insulin analog is an N-acylated Lys^{B29} insulin analog in which the amino acid residue at position B30 is Thr, Ala or deleted.

58. (Once Amended) The composition of claim 27, wherein the composition comprises about 0.2 mole to about 0.7 mole of zinc per mole of fatty acid-acylated insulin or fatty acid-acylated insulin analog.

60. (Once Amended) The composition of Claim 27, wherein the fatty acid-acylated insulin is N-acylated Lys^{B29} human insulin, and wherein the fatty acid-acylated insulin analog is an N-acylated Lys^{B29} insulin analog in which the amino acid residue at position B30 is Thr, Ala or deleted.

61. (Once Amended) The composition of claim 32, wherein the fatty acid-acylated insulin is N-myristoyl [N-palmitoyl] Lys^{B29} human insulin, and wherein the solution comprises from about 0.3 mole to about 0.55 mole of zinc per mole of fatty acid-acylated insulin.

64. (Once Amended) The composition of claim 63, wherein the phenolic [preservative] compound is selected from the group consisting of phenol and m-cresol.

65. (New) The composition of Claim 27, wherein the fatty acid in the fatty acid-acylated analog is myristic acid.

66. (New) The composition of Claim 28, wherein the fatty acid in the fatty acid-acylated analog is myristic acid.

67. (New) The composition of claim 58, wherein the pH is 6.8 to 7.8.

PENDING CLAIMS

27. (Once Amended) A composition comprising

(a) a fatty acid-acylated insulin or a fatty acid-acylated insulin analog in which the amino acid residue at position B30 is Thr, Ala or deleted, and

(b) zinc.

28. (Once Amended) A composition comprising an aqueous solution of

(a) a fatty acid-acylated insulin or a fatty acid-acylated insulin analog in which the amino acid residue at position B30 is Thr, Ala or deleted, and

(b) zinc.

29. (Once Amended) The composition of Claim 28, wherein the solution comprises about 0.2 mole to about 0.7 mole of zinc per mole of fatty acid-acylated insulin or fatty acid-acylated insulin analog.

30. The composition of Claim 29, wherein the pH is 6.8 to 7.8.

31. (Once Amended) The composition of Claim 30, further comprising a phenolic compound at a concentration of from 0.5 mg to 5 mg per milliliter of the aqueous solution.

32. (Once Amended) The composition of Claim 31, wherein the fatty acid-acylated insulin is N-acylated Lys^{B29} human insulin, and wherein the fatty acid-acylated insulin analog is an N-acylated Lys^{B29} insulin analog in which the amino acid residue at position B30 is Thr, Ala or deleted.

57. The composition of claim 28, wherein the composition is a pharmaceutical composition that further comprises a phenolic compound, glycerol, and a pharmaceutically acceptable buffer.

58. (Once Amended) The composition of claim 27, wherein the composition comprises about 0.2 mole to about 0.7 mole of zinc per mole of fatty acid-acylated insulin or fatty acid-acylated insulin analog.

60. (Once Amended) The composition of Claim 27, wherein the fatty acid-acylated insulin is N-acylated Lys^{B29} human insulin, and wherein the fatty acid-acylated insulin analog is an N-acylated Lys^{B29} insulin analog in which the amino acid residue at position B30 is Thr, Ala or deleted.

61. (Once Amended) The composition of claim 32, wherein the fatty acid-acylated insulin is N-myristoyl Lys^{B29} human insulin, and wherein the solution comprises from about 0.3 mole to about 0.55 mole of zinc per mole of fatty acid-acylated insulin.

62. The composition of claim 61, wherein the concentration of phenolic compound is from about 2.5 mg to about 5.0 mg per milliliter of the aqueous solution.

63. The composition of claim 62, wherein the phenolic compound is selected from the group consisting of phenol, m-cresol, p-cresol, o-cresol, methylparaben, and mixtures thereof.

64. (Once Amended) The composition of claim 63, wherein the phenolic compound is selected from the group consisting of phenol and m-cresol.

65. (New) The composition of Claim 27, wherein the fatty acid in the fatty acid-acylated analog is myristic acid.

66. (New) The composition of Claim 28, wherein the fatty acid in the fatty acid-acylated analog is myristic acid.

67. (New) The composition of claim 58, wherein the pH is 6.8 to 7.8.